THE EFFECT OF FEEDING MALTULOSE AND LACTULOSE ON HEPATIC LIPOGENIC ENZYME ACTIVITIES IN THE RAT.

ABSTRACT

The effect of feeding maltulose, lactulose, and sucrose (ketose disaccharides) and maltose and lactose (aldose disaccharides) on hepatic lipogenic enzyme activities in the rat was studied. Male Sprague-Dawley rats were starved for 2 days and refed for 2 days diets containing 45% total carbohydrate. Lactulose and lactose were fed at a level of 15% of the diet due to their poor digestibility. Activities of hepatic glucose-6-phosphate dehydrogenase (G6PD) and malic enzyme (ME) were measured. Hepatic G6PD and ME activities in rats fed maltulose were similar to rats fed maltose. Hepatic ME activity was lower in rats fed maltulose than sucrose. Rats fed lactulose had lower G6PD and ME activities than rats fed lactose. The study suggests that in the rat lactulose is less utilizable than lactose, and that maltulose is less lipogenic than sucrose.

Keywords: Ketose Disaccharides . Lipogenic Response . Digestability

INTRODUCTION

Maltulose and lactulose are ketose analogs of maltose and lactose, and are present in very small quantities in certain foods (1-3). Both sugars exhibit similar properties, e.g., high solubility and moderate sweetness (4-6). With currently available technology these ketose disaccharides have the potential of being produced in large quantities from agricultural by-products (4, 7, 8).

Due to their specific properties and potential availability, it has been suggested that maltulose and lactulose might have important applications for the food industry (6, 7). However, only limited studies have been conducted on the metabolism of these sugars in mammals (9-11).

The present study was conducted to measure the relative lipogenicity of these ketose disaccharides in rat liver.

MATERIALS AND METHODS

Two separate diet studies were conducted with 5 to 6 week old male Sprague-Dawley rats obtained from Hilltop Lab Animals, Inc., Scottdale, Pennsylvania. Rats were housed individually in stainless steel cages. Periods of light (0900 to 2100 hours) and dark (2100 to 0900 hours) were controlled by an automatic clock in a room with controlled temperature (21 to 25°C) and humidity (40 to 50%). Rats were equilibrated with rodent laboratory chow (Purina #5001) for 3 days prior to dietary manipulation. Following equilibration, rats were subjected to 2 days of starvation followed by feeding of the experimental diets for 2 days. This starvation-refeeding regimen was used, since in previous work it was shown to be relatively sensitive to the lipogenic tendency of various carbohydrates and to their digestibility (12-14).

Diets contained 45% total carbohydrate, 36% vitamin-free casein, 5% corn oil, 5% water, 4.9% cellulose, 3.1% AIN salt mix (15) (prepared without sucrose), and 1% vitamin fortification mix (# 40060, Teklad Test Diets, Madison, Wisconsin). Maltulose (4-O-α-D-glucopyranosyl-D-fructose) was prepared as an amorphous solid (3) and then purified (8). The maltulose preparation contained 98.3% sugars (89% maltulose, 7% maltose, 2% glucose and 0.3% fructose) and 1.7% moisture and other compounds. Lactulose (4-O-β-D-galactopyranosyl-D-fructose) was prepared (8, 16) and crystallized to analytical purity. Maltose, sucrose and lactose were obtained from commercial sources. Lactulose and lactose were fed at only a 15% level (plus 30% glucose) due to their poor digestibility (9, 10, 14). Digestibility of the sugars fed was ascertained by physical appearance of the cecum and intestines and lack of diarrhea (13, 14).

Nonfasted rats were killed in the early part of the light cycle by decapitation, and the livers were quickly removed, chilled over ice-cold glass and weighed. A 1.0 g sample of liver was used for the assay of glucose-6-phosphate dehydrogenase (G6PD, EC 1.1.1.49) and malic enzyme (ME, EC 1.1.1.40) (17). Enzyme activity is expressed as units per 100 g of final body weight. One unit of enzyme activity is defined as that amount of enzyme producing 1 μmole of measured product per minute under the conditions of the assay. The justification for expressing enzyme activity as units per 100 g of body weight has been previously given (12, 17, 18). Relative liver size = (wet liver wt. x 100)/(final body weight). Food intake is expressed as g/2 days/100 g of original body weight. Differences were tested by a one-way ANOVA and Duncan's multible range test. Differences with P values less than 0.05 were considered to be statistically significant.

RESULTS

In experiment #1, hepatic G6PD and ME activities, relative liver size, food intake and percent weight gain were similar for rats fed maltulose or maltose (Table I). Rats fed maltulose had lower hepatic ME activity and consumed less food than did rats fed sucrose. The appearance of the cecum and intestines was similar in rats fed maltulose, maltose or sucrose.

In experiment #2, hepatic G6PD and ME activities, relative liver size and percent weight gain were reduced to a greater extent in rats fed lactulose than lactose (Table I). Rats fed lactose were observed to have some gaseous distention of the cecum and large intestine, whereas rats fed lactulose had marked distention of the cecum and large intestine and exhibited diarrhea.

TABLE 1

Effect of Diets Containing Ketose and Aldose Disaccharides on Rat Liver Lipogenic Enzyme Activities, Liver Size, Food Intake, and Body Weight

Diet fed[1]	Glucose-6-phosphate dehydrogenase	Malic enzyme	Relative liver size	Food intake	Weight Gain
	U/100 g body weight		%	g/2 days/100 g body weight	%
Experiment #1					
45% maltulose preparation[2]	64[3] ± 6.9[a]	30 ± 5.3[a]	5.6 ± 0.18[a]	23.0 ± 0.43[a]	20.2 ± 0.61[a]
45% maltose	63 ± 7.3[a]	29 ± 5.7[a]	5.5 ± 0.15[a]	24.5 ± 0.74[a,b]	22.4 ± 1.06[a]
45% sucrose	79 ± 9.1[a]	46 ± 5.7[b]	5.9 ± 0.16[a]	25.1 ± 0.47[b]	21.9 ± 0.95[a]
Experiment #2					
15% lactulose[4] + 30% glucose	29 ± 3.1[x]	16 ± 2.5[x]	5.1 ± 0.19[x]	26.9 ± 0.76[x]	19.1 ± 0.69[x]
15% lactose[4] + 30% glucose	46 ± 5.7[y]	25 ± 2.6[y]	5.8 ± 0.15[y]	28.7 ± 1.06[x]	24.4 ± 1.52[y]

[1] Male rats (176 ± 1.6 g) were starved for 2 days and refed for 2 days.

[2] The maltulose preparation contained 98.3% sugars (89% maltulose, 7% maltose, 2% glucose, and 0.3% fructose) and 1.7% moisture and other compounds.

[3] Each mean represents the average of 8 rats ± SEM. Within experiment and parameter, means not sharing a common superscript letter are significantly different ($P < 0.05$).

[4] Lactulose and lactose were fed at a 15% level due to their poor digestibility.

DISCUSSION

The present study supports the findings of an earlier in vitro experiment which reported that the ketose disaccharide maltulose, but not lactulose, was hydrolyzed by mucosal enzymes from rat small intestine (10). The appearence of the intestines and cecum of these rats (13, 14) suggests that maltulose is digested by the small intestine of the rat when fed at a relatively high level (40% of the diet) and that lactulose is not digested even when fed at a relatively low level (15% of the diet).

The study further suggests that maltulose maybe less lipogenic than sucrose, since hepatic ME activity was lower in rats fed maltulose than sucrose (Table 1). This difference in lipogenic enzyme activity cannot be readily explained by the observation that rats fed maltulose consumed 8% less food than rats fed sucrose. In previous experiments where there was a comparable reduction in food intake, an appreciable reduction in hepatic G6PD and ME activities was not seen (19, 20).

Since maltulose appears to be less lipogenic than sucrose, and is reported to be less cariogenic than glucose, maltose or lactose[1], this ketose disaccharide might have potential use as a substitute sweetener for sucrose, as well as, a humectant for intermediate moisture foods. However, no studies have been conducted to directly assess the digestibility and metabolism of maltulose in human subjects.

In contrast to maltulose, lactulose is not hydrolyzed in the small intestine of rat or man (9, 10), and therefore cannot be consumed in large quantities without inducing diarrhea. However, since lactulose is noncaloric and exhibits low cariogenicity[1] (21), this ketose disaccharide could have potential application in specialty foods, e.g. chewing gum, where it is consumed only in small amounts. Lactulose may also have additional health benefits due to its ability to create an acidic environment within the colon (11, 22).

Footnotes

1. Unpublished data. K.B. Hicks and G. Somkuti. Eastern Regional Research Service, ARS, USDA, Philadelphia, PA.

REFERENCES

1. Engel CE, Olinger PM. High pressure liquid chromatographic determination of saccharides in corn sirups: Collaborative study. J. Assoc. Off. Anal. Chem. 1979; 62:527-32.
2. Doner LW. The sugars of honey - a review. J. Sci. Fd. Agric. 1977; 28:443-56.
3. Geier H, Klostermyer H. Formation of lactulose during heat treatment of milk. Milchwissenschaft 1983; 38:475-7.
4. Hicks KB, Symanski EV, Pfeffer PE. Synthesis and high-performance liquid chromatography of maltulose and cellobiulose. Carbohydr. Res. 1983; 112:37-50.
5. Lee CK, Birch GG. Structural functions of taste in the sugar series VII: Taste properties of Ketoses. J. Pharm. Sci. 1976; 65:1222-5.
6. Parrish FW, Talley FB, Ross KD, Clark J, Phillips JG. Sweetness of lactulose relative to sucrose. J. Food Science 1979; 44: 813-5.

7. Hodge JE, Rendleman JA, Nelson EC. Useful properties of maltose. Cereal Science Today 1972; 17:180-8.
8. Hicks KB, Raupp DL, Smith PW. Preparation and purification of lactulose from sweet cheese whey ultrafiltrate. J. Agric. Food Chem. 1984; 32:288-92.
9. Dahlqvist A, Gryboski JD. Inability of the human small-intestinal lactase to hydrolyze lactulose. Biochim. Biophys. Acta 1965; 110:635-6.
10. Ruttloff H, Taeufel A, Krause W, Haenel H, Taeufel K. The intestinal enzymic decomposition of galactose oligosaccharides in the human and animal intestine, with particular regard to lactobacillus bifidus. II. On the intestinal behavior of lactulose. Nahrung 1967; 11:39 (GER); cf. C. A. 1967; 67:41636p.
11. Mendez A, Olano A. Lactulose. A review of some chemical properties and applications in infant nutrition and medicine. Dairy Sci. Absts. 1979; 41:531-5.
12. Michaelis OE, IV, Szepesi B. Effect of various sugars on hepatic glucose-6-phosphate dehydrogenase, malic enzyme and total liver lipid of the rat. J. Nutr. 1973; 103:697-705.
13. Michaelis OE, IV, Nace CS, Szepesi B. Effect of refeeding raw and cooked starches on hepatic enzyme activities of rats. Br. J. Nutr. 1978; 39:85-9.
14. Michaelis OE, IV, Szepesi B. Effect of galactose containing disaccharides and trisaccharides on hepatic enzyme responses in starved-refed rats. Nutr. Rep. Int. 1976; 14:553-9.
15. Report of the America Institute of Nutrition Ad Hoc Committee on Standards for Nutritional Studies. J. Nutr. 1977; 107: 1340-8.
16. Hicks KB, Parrish FW. A new method for the preparation of lactulose from lactose. Carbohydr. Res. 1980; 82:393-7.
17. Freedland RA. Effects of progressive starvation on rat liver enzyme activities. J. Nutr. 1967; 91:489-95.
18. Szepesi B. "Metabolic Memory": Effect of antecedent dietary manipulations on subsequent diet-induced response of rats. I. Effects on body weight, food intakes, glucose-6-phosphate dehydrogenase, and malic enzyme. Can. J. Biochem. 1973; 51:1604-16.
19. Szepesi B, Freedland RA. Differential requirement for de novo RNA synthesis in the starved-refed rat; inhibition of the overshoot by 8-azaguanine after refeeding. J. Nutr. 1969; 99:449-58.
20. Szepesi B, Berdanier CD, Diachenko SK, Moser PB. Effect of length of starvation, refeeding, and 8-azaguanine on serum insulin and NADP-linked dehydrogenases of rat liver. J. Nutr. 1971; 101:1147-52.
21. Makinen KK, Rekola M. Comparison between sucrose and lactulose in a suspended salivary system. J. Dent. Res. 1975; 54:1244
22. Samuelson SL, Nelson RL, Nyhus LM. Protective role of faecal pH in experimental colon carcinogenesis. J. Royal Soc. Med. 1985; 78:230-33.